

paragraph, as being non-enabled. In particular, the Examiner has asserted that the specification does not reasonably provide enablement for (1) an antibody that binds an Apo-2 DcR polypeptide which is not identical to SEQ ID NO:1; (2) an antibody which binds Apo-2 DcR and which is a blocking antibody; or (3) a hybridoma cell line producing either the antibody of (1) or (2). Applicants respectfully disagree.

Applicants' specification provides a detailed description and characterization of the newly identified member of the Tumor Necrosis Factor Receptor family called "Apo-2 DcR". The specification also clearly provides methods and techniques by which one of ordinary skill in the art can make or identify variants of Apo-2 DcR, including polypeptides which have a particular % amino acid sequence identity to the native sequence Apo-2 DcR polypeptide. The specification further clearly provides ample description as to how such Apo-2 DcR polypeptides can be employed to make and identify antibodies directed against such antigens. Given the extent of the disclosure in the application and the level of skill in the art, it is submitted that no undue experimentation would be required to achieve Apo-2 DcR antibodies which bind an Apo-2 DcR polypeptide having the recited structural characteristics in the present claims.

It is also submitted that anti-Apo-2 DcR blocking antibodies are enabled by the specification. As stated above, the specification provides a detailed characterization of the Apo-2 DcR polypeptide receptor. A ligand for this receptor, called Apo-2 ligand or TRAIL, is also taught. As the Examiner has even noted, the specification provides working examples showing that binding of the Apo-2 ligand to the Apo-2 DcR can inhibit apoptotic activity of the ligand. Those skilled in the art, using routine skill and assay formats known in the art, can readily use the materials taught by the specification to screen for Apo-2 DcR antibodies which exhibit blocking activity. And while, in some instances, such screening methods may involve some degree of time or experimentation, the nature of that time or experimentation would not be considered undue by the skilled practitioner. Applicants respectfully disagree with the Examiner's statements that undue experimentation without a reasonable expectation of success would be required in view

that "so little is known about which amino acids or potential epitopes would be likely to be necessary for receptor activity". It is submitted that the nature of the blocking activity can be readily identified using routine bioassays and that such a requirement for epitope mapping of the receptor is not essential for purposes of making and identifying the claimed antibodies.

For all these reasons, withdrawal of the Section 112, first paragraph rejections, is respectfully requested.

Claims 15, 17-24, 51, and dependent claims 16, 25-28, 50 and 52 were rejected under Section 112, second paragraph, as being indefinite. Each of these rejections are discussed below.

Claim 15 has been rejected on the basis that the term "binds" is not clear. Applicants respectfully traverse this rejection on the grounds that the term "binds" as used in the antibody arts is one which is fully understood by the skilled practitioner. The term is used in a general sense, and those persons of ordinary skill in this art will readily understand that the term as used is not meant to be unduly limited so as to only refer to a single type of binding such as direct or indirect binding, as suggested by the Examiner.

Claim 15 has also been rejected with respect to the sequence identity language in the claim. As shown above, claim 15 has been amended to further clarify that the sequence identity language is used as a modifier with respect to the polypeptide of (a) in the claim. It is believed that this amendment overcomes this indefiniteness rejection and does not effect the scope of the claim as originally presented. Applicants do wish to point out that, contrary to the Examiner's statement, basis for the % sequence identity language for both full length forms of Apo-2 DcR and particular domain forms of Apo-2 DcR can be found in the specification on at least page 14, lines 6-19.

Claims 17-21 were also rejected as being unclear. The subject claims have been amended, as shown above, pursuant to the Examiner's request. This amendment is being made to address this indefiniteness rejection and is not intended to effect the scope of the claims as originally presented.

Claims 22-24 were rejected as being indefinite on the grounds that

the term "biological characteristics" is unclear. Applicants respectfully disagree and point out that the term as used in the claim is clearly defined on page 54. However, in an effort to advance the prosecution of the claims, Applicants have amended the language in the claims to even more clearly recite the characteristics provided for in this definition.

Claim 51 was also rejected as being indefinite. Applicants have amended the claim in the above amendment to further clarify the language in the claim along the lines suggested by the Examiner. This amended language is supported by the specification on at least page 61.

Lastly, Applicants wish to address certain comments included under the sections entitled "Prior Art" and "Term Usage" on page 7 of the office action. First, the Examiner has stated that "while provisional priority application 60/049,911 discloses the complete Apo-2DcR protein and encoding nucleic acid, it does not disclose a specific antibody..." Applicants wish to make clear for the record that Applicants' priority provisional application provides a complete and enabling disclosure regarding anti-Apo-2DcR antibodies. It is believed that the Examiner's statement should be construed only to indicate that certain working examples concerning some ATCC deposited antibodies were added at the time of filing Applicants' non-provisional application. Second, in addition to the noted terms used in the art to refer to polypeptides related to Apo-2DcR, Applicants wish to advise that the terms "TRAIL-BP", "hApo-9" and "TNFR-5" have also been employed. These various terms have been employed, for instance, in the published patent application documents recently cited in Applicants' supplement information disclosure statement.

Respectfully submitted,

GENENTECH, INC.

Date: June 29, 2000

By: *Diane L. Marschang*
Diane L. Marschang
Reg. No. 35,600

1 DNA Way
So. San Francisco, CA 94080-4990
Phone: (650) 225-5416
Fax: (650) 952-9881